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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/904,838	07/13/2001	Avi Ashkenazi	10466/72	5331

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HELLER EHRMAN LLP
275 MIDDLEFIELD ROAD
MENLO PARK, CA 94025-3506

EXAMINER	
ROMEO, DAVID S	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 06/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/904,838	ASHKENAZI ET AL.	
	Examiner	Art Unit	
	David S. Romeo	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 March 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44-46 and 49-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44-46, 49-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

5.00

DETAILED ACTION

The amendment filed 03/21/2005 has been entered. Claims 44-46, 49-51 are pending and being examined.

Maintained Formal Matters, Objections, and/or Rejections:

Priority

The present claims are directed to or encompass a polypeptide comprising the amino acid sequence of SEQ ID NO: 114. Based on the priority statement filed August 26, 2002 and an inspection of the patent applications, the examiner has concluded that the claimed subject matter is supported by the disclosure in application serial no. PCT/US00/04414, filed February 22, 2000 but is not supported by any of the others because the claimed subject matter is not supported in the manner provided by 35 U.S.C. 112, first paragraph in any of the earlier filed applications.

Applicants argue that Pennica teaches nothing regarding a lack of correlation of DNA and protein, in genes in general, that the utility guidelines require only require that it is more likely than not that a correlation exists, and that Pennica cannot be used against Applicants. Applicant's arguments have been fully considered but they are not persuasive. Pennica is evidence that not all gene amplifications are associated with overexpression of the corresponding gene product and that the skilled artisan would not have appreciated that PRO317 gene amplification, without more, would have suggested a specific and substantial patentable utility for the PRO317 polypeptide. The examiner is not arguing that a correlation between PRO317 gene amplification and PRO717 polypeptide expression does not exist. The examiner is arguing that the present specification fails to disclose what that correlation is or the significance of any

such correlation. The specification fails to disclose enough information about the invention to make its usefulness immediately apparent to those familiar with the technological field of the invention.

Applicants argue that Dr. Polakis's statements are reasonable and accurate, and therefore the examiner's request for evidentiary support is improper. Applicant's arguments have been fully considered but they are not persuasive. The examiner did not request evidentiary support for the statements made by Dr. Polakis in the declaration under 37 CFR 1.132 filed 06/28/2004. The examiner did say that the declaration does not provide data such that the examiner can independently draw conclusions. Only Dr. Polakis' conclusions are provided in the declaration. There is no evidentiary support to Dr. Polakis' statement that it remains a central dogma in molecular biology that increased mRNA levels are predictive of corresponding increased levels of the encoded protein. Furthermore, the utility guidelines [Federal Register: January 5, 2001 (Volume 66, Number 4), Part IIB, pages 1098-1099] remind Office personnel:

> "that they must treat as true a statement of fact made by an applicant in relation to an asserted utility, unless countervailing evidence can be provided that shows that one of ordinary skill in the art would have a legitimate basis to doubt the credibility of such a statement. Similarly, Office personnel must accept an opinion from a qualified expert that is based upon relevant facts whose accuracy is not being questioned; it is improper to disregard the opinion solely because of a disagreement over the significance or meaning of the facts offered." Part IIB.

Pennica is evidence that not all gene amplifications are associated with overexpression of the corresponding gene product and that the skilled artisan would not have appreciated that PRO317 gene amplification, without more, would have suggested a specific and substantial patentable utility for the PRO317 polypeptide. Pennica also provides countervailing evidence that the skilled artisan would have a legitimate basis to doubt the utility of the PRO317 polypeptide.

Haynes and Hancock provide evidence that that Dr. Polakis' asserted dogma is not absolutely true.

Applicants do not agree that Haynes and Hancock contradict the Polakis declaration because Haynes found that there was a general trend and because Haynes's teaching that protein levels cannot be accurately predicted From mRNA levels is not the same as there being no correlation between protein and mRNA. Applicants argue that Haynes supports the Polakis declaration because the Haynes data support the "more likely than not" utility standard. Applicants argue that the examiner has not shown that a lack of correlation between gene amplification and polypeptide over-expression is typical, that Pennica, Haynes, or Hancock show that it is more likely than not that gene amplification is not correlated with polypeptide over-expression, that the standard for utility is not absolute certainty, that the gene amplification data provides a specific benefit in currently available form, that the skilled artisan would know how to use the claimed polypeptides for the diagnosis of lung or colon cancer, and therefore Applicants are entitled to a priority date of September 10, 1998. Applicant's arguments have been fully considered but they are not persuasive. First, the present specification provides no information regarding increased mRNA levels of PRO317 in tumor samples relative to normal samples. Only gene amplification data was presented. Second, Although Haynes states:

> "Interpretation of quantitative mRNA expression profiles frequently implicitly or explicitly assume that for specific genes the transcript levels are indicative of the levels of protein expression" (page 1863, left column, full paragraph 1),

Haynes goes on to state:

> "These results suggest that even for a population of genes predicted to be relatively homogenous ..., the protein levels cannot be accurately predicted from the level of the corresponding mRNA transcript" (page 1863, left column, full paragraph 1).

Haynes concludes that the protein levels cannot be accurately predicted from the level of the corresponding mRNA transcript. Haynes provides evidence that protein expression levels are not predictable from the mRNA expression levels. Haynes cites this lack of predictability as one of the main reasons for proteome analysis to become an essential component in the comprehensive analysis of biological systems. Paragraph bridging pages 1862-1863; page 1863, left column, full paragraph 1. Haynes further teaches that:

> "it is evident that the analysis of mature protein products in cells is essential as there are numerous levels of control of protein synthesis, degradation, processing and modification, which are only apparent by direct protein analysis" page 1863, right column, full paragraph 2).

Hancock is consistent with Haynes. Namely, the analysis of protein products is essential because protein expression levels are not predictable from the mRNA expression levels.

In view of the fact the present specification provides no information regarding increased PRO317 mRNA levels in tumor samples relative to normal samples, in view of the fact that not all gene amplifications are associated with overexpression of the corresponding gene product, in view of the fact that protein levels cannot be accurately predicted from the level of the corresponding mRNA transcript, in view of the fact that there are numerous levels of control of protein synthesis, degradation, processing and modification, which are only apparent by direct protein analysis, and in view of the fact the present specification provides no information regarding the expression, role or activity of the PRO317 polypeptide in cancer, there is no basis for concluding that the skilled artisan would conclude that it would be more likely than not the PRO317 polypeptide could be used as a cancer diagnostic or therapeutic because the skilled artisan would not know if PRO317 polypeptide levels would be upregulated, downregulated, or

unchanged in caner. The examiner is not arguing that a correlation between PRO317 gene amplification and PRO717 polypeptide expression does not exist. The examiner is arguing that the present specification fails to disclose what that correlation is or the significance of any such correlation. The specification fails to disclose enough information about the invention to make its usefulness immediately apparent to those familiar with the technological field of the invention.

Claim Rejections - 35 USC § 102

Claims 44-46, 49-51 are rejected under 35 U.S.C. 102(a) as being anticipated by Ruben (N, WO 99/09198).

Applicants argue that they are entitled to an effective filing date of at least September 10, 1998 because the gene amplification data in the priority application PCT/US98/18824 provides a specific benefit in currently available form for the claimed PRO317 polypeptide. Applicant's arguments have been fully considered but they are not persuasive for the reasons discussed above.

Information Disclosure Statement

Note that the IDS filed March 14, 2002 was initialed by the examiner and a copy was provided to Applicant in the Office action mailed 09/09/2003. The "Other Art" in the IDS filed March 14, 2002 will be printed on a resulting patent exactly as it was provided, i.e., "Blast Results A1-A16, GenBank" and "Blast Results, B1-B9, Dayhoff."

Conclusion

No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (571) 272-0890. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M. IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, BRENDA BRUMBACK, CAN BE REACHED ON (571) 272-0961.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE CENTRAL FAX NUMBER FOR OFFICIAL CORRESPONDENCE, WHICH IS (571) 273-8300.

CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (571) 273-0890.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.

David Romeo

DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

DSR
JUNE 11, 2005